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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,788	10/17/2003	Shamci Monajembashi	SHA-001	9873

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EXAMINER	
WHALEY, PABLO S	
ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
07/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/687,788	**Applicant(s)** MONAJEMBASHI, SHAMCI	
	Examiner Pablo Whaley	**Art Unit** 1631	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 June 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *16-19, 21, 24-26, 28, and 29*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 11. does NOT place the application in condition for allowance because:

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
Applicant's arguments, filed 06/15/2007, are persuasive. This rejection is hereby withdrawn.

Claims 16-19, 21, 24-26, and 28 are rejected under 35 U.S.C. 103(a) as being made obvious by Henon et al. (Biophysical Journal, 1999, Vol. 76, p.1145-1151), in view of Jan et al. (THE JOURNAL OF GENERAL PHYSIOLOGY, 1973, Vol. 61, p. 638-654). This rejection is necessitated by amendment.

Applicant's arguments, filed 06/15/2007, regarding the teachings of Henon et al. and Jan et al. are not persuasive for the following reasons.
As set forth in the previous office action, mailed 02/15/2007, Henon et al. teach a method of adhering at least one erythrocytes (i.e. target cell) bound to silica beads (i.e. auxillary object) [Abstract], as in instant claims 16 and 18. It is noted that claim 16 requires "adhering to at least one auxillary object. Henon et al. do not specifically teach adhering erythrocytes to "target cells" or coating objects with substances, as in instant claims 16 and 17. However, Henon et al. suggest coating RBCs with buffers to improve cell geometry [p.1145, Materials and Methods].
Jan et al. teach a method for aggregating RBCs (i.e. adherent objects) using Dextran, which functions to change the surface charge of the erythrocytes resulting in aggregation [Abstract]. The Examiner has broadly and reasonably interpreted this as a teaching for "adhering" multiple cells together using a substance that changes surface charge, as in claims17. Jan et al. also teach fixing of RBCs [p.641, Section 8], as in claim 18.

For these reasons, the Examiner maintains that it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the Dextran-induced cell aggregation method taught by Jan et al. in combination with the optical tweezer method and system of Henon et al., where the motivation would have been to further investigate methods for inhibiting red blood cell aggregation [Jan et al., Abstract and p.652 2] or to further investigate viscoelastic properties of aggregated RBCs [Henon et al., Conclusion], resulting in the practice of the instant claimed invention. One of skill in the art would have had a reasonable expectation of successfully combing these methods as both teach methods for analyzing erythrocytes in vitro and measuring shear forces experimentally.

Applicant's arguments that appear to be directed to unexpected results of RBCs and other auxilliary objects being superior to beads are not persuasive for the following reasons. It is well settled that unexpected results must be established by factual evidence. Applicant's have not presented any experimental data that the use of RBCs or other auxilliary objects results in an unexpected advantage. Due to the absence of such data, applicant's assertion of unexpected results constitute mere argument. See also In re Linder, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972; Ex parte George, 21 USPQ2d 1058 (Bd. Pat. Appl. & Inter. 1991).

Claims 16-19, 21, 24-26, 28 and 29 are rejected under 35 U.S.C. 103(a) as being made obvious by Visscher et al. (Cytometry, 1993, Vol. 14, p.105-114), in view of Jan et al. (THE JOURNAL OF GENERAL PHYSIOLOGY, 1973, Vol. 61, p. 638-654) and Shaw et al. (Cellular Microbiology, 2001, Vol. 3, No. 4, p.213-222). This rejection is necessitated by amendment.

Applicant's arguments, filed 06/15/2007, regarding the combination and teachings of Visscher et al.,Jan et al. , and Shaw et al. are not persuasive for the following reasons.

As set forth in the previous office action, mailed. 2/15/2007, Visscher et al. teach a method and system for inducing optical forces for manipulating a target comprising a microscope, multiple beams, optical tweezers, and long wave beams [Fig. 1], [p.106, Col. 2, 3], and [p.112, Col. 2, 2], as in claims 16, 19, 21, 24-26, and 28. Visscher et al. also teach unique multi-trap technique for indirectly trapping biological objects using optical tweezers, multiple cells, and polystyrene coated beads [p.113, Col. 1, 4 and Col. 2, 1] and [Fig. 7], as in claim 16. Visscher et al. also teach the use of a confocal scanning laser microscope for the micromanipulation of bacterial cells [Abstract], as in instant claim 29.
The Examiner acknowledged that Visscher et al. do not specifically teach methods for adhering auxiliary cells to erythrocytes using substances that change the surface charge of the erythrocytes [Abstract], as in claim 17. However, Visscher et al. do teach the coating of beads with specific cell binding antibodies to improve trapping [p.113, Col. 2, 1], which suggests the coating of cells using adherent substances.
Applicant's arguments that Jan et al. do not teach a method for adhering cells are not persuasive for reasons set for above, as the Examiner maintains that Jan et al. teach methods for adhering erythrocytes to other erythrocytes using substances that change the surface charge of the erythrocytes [Abstract], as in claims 16, 17, and 18. Jan et al. also teach the use of electron microscopic studies to analyze erythrocyte surface interaction [p.646, Section 3], which motivates the use of confocal microscopy. Jan et al. also teach fixing of RBCs [p.641, Section 8], as in claim 18.

For these reasons, the Examiner maintains it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the Dextran-induced cell aggregation method taught by Jan et al. in combination with with the bacterial cells and the cell trapping method of Visscher et al., where the motivation would have been to study cell-bacterial interaction by trapping irregular shaped bacteria using multiple erythrocytes [Visscher et al., p.113, Col. 1, 3], resulting in the practice of the instant claimed invention. One of skill in the art would have had a reasonable expectation of successfully using bacterial cells and the multi-trap system of

Visscher et al. with the erythrocytes of Jan et al. methods for studying erythrocyte and red blood cell interaction are well known in the art [Shaw et al., Abstract].

CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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7/23/07

ARGUMENTS

~~Remarks~~

Section 112, 2nd Paragraph

Claim 18 was found indefinite. Specifically, claim 18 is found to recite the limitation "fixed erythrocyte". The Office action noted that it "is unclear in what way said erythrocyte is "fixed" and what exactly it is fixed to, as the instant claims do not recite any methods steps directed to fixing erythrocytes."

A fixed cell (such as an erythrocyte) is a very well known term. McGraw-Hill Dictionary of Scientific and Technical Terms, Sixth Edition defines "fix" as: "To kill, harden or preserve a tissue, organ, or organism by immersion in dilute acids, alcohol, or solutions of coagulants." In Molecular Biology of the Cell, 2nd Edition, notes "fixation makes cells permeable to staining reagents and cross-links their macromolecules so that they are stabilized and locked in position. Some of the earliest procedures involved immersion in acids or in organic solvents such as alcohol. Current procedures usually include treatment with reactive aldehydes, particularly formaldehyde and glutaraldehyde, which form covalent bonds with the free amino groups of proteins and thereby cross link adjacent molecules."

These definitions of the term "fixed" are consistent with how the applicant has used the term in the specification. For example, on page 6, the applicants note, "it is possible to work with fixed erythrocytes (conserved using formaldehyde or glutaraldehyde) as well as unfixed (native) ones. From a practical point of view it is advised to work with fixed erythrocytes (one single fixation step sufficient for a couple of experiments)."